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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,595	10/19/2005	Steven Ledbetter	07680.0023-00000	6062

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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/553,595	LEDBETTER ET AL.	
	Examiner	Art Unit	
	David S. Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-38* is/are pending in the application.

4a) Of the above claim(s) *9,11,12,20,21,27,31,33 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10,13-19,22-26,28-30,32 and 35-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-38* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed 03/10/2008 has been entered. Claims 1–38 are pending.

Election/Restrictions

Applicant's election of an anti-TGFβ antibody in the reply filed on 03/10/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant's election with traverse of 1D11, lisinopril and renal insufficiency in the reply filed on 03/10/2008 is acknowledged. The traversal is on the ground(s) that the ISR found no relevant references of the X type, the Y references are not applicable under 35 U.S.C. § 102(b), no reasoned statement is provided regarding destruction of "the single general inventive concept" and there would be no undue burden to search 1D11 and CAT192. This is not found persuasive because the international search report filed with the present application indicates that the species cannot be considered novel or cannot be considered to involve an inventive concept. Search burden is not germane to restriction under PCT rule 13.1.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 11, 12, 20, 21, 27, 31, 33 and 34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/10/2008.

Specification

The disclosure is objected to because of the following informalities: The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Double Patenting

Applicant is advised that should claim 22 be found allowable, claim 36 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1–5, 13, 16–19, 22–26 and 35–38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treatment comprising administering a TGFβ antagonist and a RAAS antagonist wherein the TGFβ antagonists is an anti-TGFβ antibody and wherein the RAAS antagonist is lisinopril, does not reasonably provide enablement for said method of treatment comprising administering a TGFβ antagonist and a RAAS antagonist. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are directed to or encompass a "TGFβ antagonist" and a "RAAS antagonist." According to the specification,

> [0015] TGF-β antagonists, used in the methods of the present invention, include but are not limited to antibodies directed against one or more isoforms of TGF-β, antibodies directed against TGF-β receptors; soluble TGF-β receptors and fragments thereof; and TGF-β inhibiting sugars and proteoglycans.
>
> [0016] RAAS antagonists, used in the methods of the invention, include but are not limited to renin inhibitors, angiotensin-converting enzyme (ACE) inhibitors, and Ang II receptor antagonists.
>
> 0045] Examples of TGFβ antagonists that may be used in the methods of the present invention include … any mutants, fragments, or derivatives of the above-identified molecules that retain the ability to directly inhibit the biological activity of TGFβ.

Although the specification discloses particular antagonists, the genus of TGFβ antagonists and the genus of RAAS antagonist used in the claimed methods are structurally unlimited. The disclosure of these particular antagonists might justify a generic claim encompassing these and similar antagonists. However, it is inadequate to support for claims encompassing every possible such antagonists because the specification does not enable one to make structurally dissimilar compounds with the desired activity. In practicing the invention in a manner commensurate with the scope of the claim, a skilled artisan is left to randomly procure every conceivable compound and through trial and error experimentation is left to determine if it functions as the desired antagonists. Such random, trial and error experimentation is considered undue. Furthermore, the specification does not provide the guidance needed to reliably make the desired antagonists that are structurally dissimilar to the particular antagonists disclosed.

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements, while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific laws; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved."

The ability to test any particular compound for antagonist activity and thereby distinguish between those compounds which meet the functional limitations from those that don't is inconsistent with the decision in Fisher.

The present specification does not provide a description of a repeatable process of producing the desired antagonists. To practice the invention in a manner consistent with the breadth of the claims would require a substantial inventive contribution on the part of a skilled practitioner which would involve the determination of the structural features constituting every possible antagonist. This additional characterization constitutes undue experimentation.

Unless one has a reasonable expectation that any one material embodiment would be more likely than not to function as antagonists or the specification provides sufficient guidance to permit one to identify those embodiments which are more likely to work than not without actually making and testing them then the present application does not support the breadth of the claims.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is indefinite because it recites the term "derivative." Because the specification does not identify that material element or combination of elements which is unique to, and, therefore, definitive of "derivative" an artisan cannot determine what additional or material limitations are placed upon a claim by the presence of this element. The metes and bounds are not clearly set forth.

Claim 32 is directed to a human derivative of the 1D11 antibody. According to the specification, 1D11 is a mouse monoclonal antibody 1D11 (page 6, [0015]), and therefore arises from mouse genes. Human antibodies arise from human genes. See, for example, Filardo (U. S. Publication No. 2008/0131915), page 9, [0077]. It is unclear when a human anti-TGFβ antibody is to be considered a derivative of the 1D11 antibody and when it is not to be considered a derivative. The metes and bounds are not clearly set forth.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1–4, 6, 13–19, 22–26, 28 and 35–38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Border (Hypertension. 1998 Jan;31(1 Pt 2):181-8) and Reeves (Proc Natl Acad Sci U S A. 2000 Jul 5;97(14):7667-9).

The claims are directed to or encompass:

> A method of treating a mammal having diminished renal function, slowing loss of renal function in a mammal having a renal disorder or improving renal function in a mammal having diminished renal function, comprising administering to the mammal a therapeutically effective amount of a TGFβ antagonist and a therapeutically effective amount of a RAAS antagonist to treat renal insufficiency, slow the loss of renal function or improve the renal function, respectively.

Border teaches:

> In animals, overexpression of transforming growth factor-beta by intravenous injection, transient gene transfer, or transgene insertion has shown that the kidney is highly susceptible to rapid fibrosis. The same seems true in human disease, where excessive transforming growth factor-beta has been demonstrated in glomerulonephritis, diabetic nephropathy, and hypertensive glomerular injury. A possible explanation for the kidney's particular susceptibility to fibrosis may be the recent discovery of biologically complex interactions between the renin-angiotensin system and transforming growth factor-β. …Interaction of the renin-angiotensin system and transforming growth factor-β has important clinical implications. The protective effect of inhibition of the renin-angiotensin system in experimental and human kidney diseases correlates closely with the suppression of transforming growth factor-β production. This suggests that transforming growth factor-β, in addition to blood pressure, should be a therapeutic target. Higher doses or different combinations of drugs that block the

> renin-angiotensin system or entirely new drug strategies may be needed to achieve a greater antifibrotic effect.

Abstract.

> …the current pharmacological approaches to block the RAS are suboptimal and that, in addition to blood pressure, normalization of TGFβ should be part of the therapeutic goal. Current evidence suggests that a combination of RAS blockade with a separate agent to suppress TGF-β may be superior to RAS blockade alone. Such a combination may be required if progressive fibrotic diseases, such as diabetic nephropathy, are to be truly prevented, instead of just delayed.

Paragraph bridging pages 181-182.

> …in renal fibrotic diseases, therapies aimed at more than one arm [of the RAS and TGFβ systems] will be necessary to effectively halt, rather than merely slow, disease.

Page 186, right column, full paragraph 1. Border also discloses enalapril, an ACE inhibitor (paragraph bridging pages 182-183), and neutralizing antibody to TGFβ (page 184, paragraph bridging left and right columns).

According to Reeves,

> Angiotensin converting enzyme inhibitors (ACE-I) slow the progression of kidney disease in both type I and type II diabetes …The inability of ACE-I treatment to completely halt the progression of diabetic nephropathy may relate to the incomplete suppression of TGF-β production by these agents. …Thus, it will be important to develop more effective approaches for suppressing TGF-β production or activity and to determine whether these approaches are more effective in halting the progression of kidney disease … .

Page 7668, right column, last full paragraph.

> …the ability of TGF-β to bind with its receptor could be reduced … by scavenging active TGF-β … with neutralizing antibodies … .

Page 7669, paragraph bridging middle and right columns.

Reeves also teaches:

> Diabetic nephropathy refers to a characteristic set of structural and functional kidney abnormalities that occur in patients with diabetes. Although best described in patients with type I diabetes …, similar findings are now known to occur in the more common type II diabetic patient …. Structural abnormalities include hypertrophy of the kidney, an increase in the thickness of glomerular basement membranes, accumulation of extracellular matrix components in the glomerulus (nodular and diffuse glomerulosclerosis), tubular atrophy, and interstitial fibrosis …. Functional alterations include an early increase in the glomerular filtration rate with intraglomerular hypertension, subsequent proteinuria, systemic hypertension, and eventual loss of renal function …. Clinicopathologic studies of diabetic nephropathy have established that the extent of matrix accumulation in both the glomeruli and the interstitium correlate strongly with the degree of renal insufficiency and proteinuria ….

Page 7667, first two paragraphs. Reeves also discloses certain human populations that are at greater risk for developing diabetic nephropathy (page 7669, right column, last paragraph). In disclosing diabetic nephropathy in diabetic patients, Reeves discloses human, diabetic and hypertensive mammals having diminished renal function and/or renal insufficiency.

Border and Reeves suggest combining a therapeutically effective amount of a TGFβ antagonist with a therapeutically effective amount of a RAAS antagonist for the treatment of a renal disorder, diminished renal function or renal insufficiency. Therefore, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat a mammal having a renal disorder or diminished renal function by administering to the mammal a therapeutically effective amount of a TGFβ antagonist and a therapeutically effective amount of a RAAS antagonist, wherein the loss of renal function is selected from the group consisting of pressure filtration, selective reabsorption, tubular secretion, and systemic blood pressure regulation, wherein the RAAS antagonist is an ACE inhibitor, wherein the TGFβ antagonist is an anti-TGFβ antibody, wherein the mammal is human, diabetic or hypertensive, wherein the mammal has renal insufficiency, with a reasonable expectation of success. One of ordinary skill

in the art would be motivated to make this modification because the current pharmacological approaches to block the RAS are suboptimal and that, in addition to blood pressure, normalization of TGFβ should be part of the therapeutic goal.

Applicants are claiming the administration of the same compounds that the prior art teaches to the same individuals that the prior art teaches for the treatment of the same conditions that the prior art teaches. Therefore, treating renal insufficiency, slowing the loss of pressure filtration, selective reabsorption, tubular secretion, and systemic blood pressure regulation, and improving pressure filtration, selective reabsorption, and tubular secretion, reduction of proteinuria by at least 10% and reduction of albumin excretion by at least 10% would flow naturally from following the suggestions of Border and Reeves.

Regarding claims 16 and 38, Border and Reeves disclose the general conditions of the claimed method(s). Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable conditions by routine experimentation. Furthermore, the normal desire of an artisan in the art of renal therapy to preserve or improve renal function as much as possible for as long as possible provides the motivation to determine the optimum length of treatment.

The invention is prima facie obvious over the prior art.

Claims 1–4, 6–8, 10, 13–19, 22–26, 28–30, 32 and 35–38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Border (Hypertension. 1998 Jan;31(1 Pt 2):181-8) and Reeves (Proc Natl Acad Sci U S A. 2000 Jul 5;97(14):7667-9) as applied to claims 1–4, 6, 13–19, 22–26, 28 and 35–38 above and further in view of Ledbetter (WO 01/66140).

Borders and Reeves teach a method of treating a mammal having diminished renal function, slowing loss of renal function in a mammal having a renal disorder or improving renal function in a mammal having diminished renal function, comprising administering to the mammal a therapeutically effective amount of a TGFß antagonist and a therapeutically effective amount of a RAAS antagonist to treat renal insufficiency, slow the loss of renal function or improve the renal function, respectively, wherein the TGFβ antagonist is an anti-TGFβ antibody.

Border and Reeves do not teach a TGFβ antagonist wherein the TGFβ antagonist is a human anti-TGFβ antibody, a humanized anti-TGFβ antibody, 1D11 or a humanized derivative of 1D11.

Ledbetter discloses a method for treating loss of renal function by administering a TGFß antagonist (page 1, lines 8-10). End stage renal failure is treatable only by dialysis or organ transplant (page 1, lines 16-17). Three physiological processes are involved in proper kidney function: pressure filtration, selective reabsoprtion, and tubular secretion (page 1, line 29 through page 2, line 12).

Typically, insults to the kidney initiate a wound repair response. Part of this response involves tissue repair and remodeling. Fibrosis occurs if tissue repair is not properly regulated. Many renal diseases and disorders exhibit concomitant fibrosis of the kidney. Ledbetter page 2, lines 19-22.

TGF-beta antagonist are useful for treating loss of kidney function occurring in the context of acute and chronic kidney disease. Antagonism of TGFß effectively slows the progression of kidney damage, e.g., by preventing loss of renal vascular circulation, reducing

tubular injury of the renal medulla, and preventing systemic hypertension. Ledbetter page 4, full paragraph 1.

It is a further object to maintain renal function, or to slow, halt or reverse loss of renal function (Ledbetter, page 5, full paragraph 3). TGFß antagonists include antibodies directed against one or more isoforms of TGFß. More preferably the TGFß antagonist is a human or humanized monoclonal antibody that blocks TGFß binding to its receptor. Most preferred, is a humanized form of the murine monoclonal antibody obtained from hybridoma 1D11.16 (ATCC Accession No. HB 9849). Ledbetter page 5, full paragraph 4; page 9, line 28 through page 10, line 28.

A TGFß antagonist significantly reduced proteinuria (Ledbetter, page 6, full paragraph 3; page 13, lines 4, 14-15; page 19, full paragraphs 1, 3) and albumin excretion (Ledbetter, page 19, full paragraphs 2, 3).

A wide variety of diseases or disorders can be treated with a TGFß antagonist (Ledbetter, page 7, line 17 through line 34).

A pharmaceutically effective amount of a TGFß antagonist is an amount sufficient to ameliorate one or more pathological processes associated with loss of renal function. The determination of a pharmaceutically acceptable amount is well within the ability of those skilled in the art. Ledbetter, page 8, full paragraph 2.

Ledbetter also discloses treatment with anti-TGFß antibody 1D11.16 (page 11, last paragraph).

Applicants' specification discloses that mouse monoclonal antibody 1D11 is also known as 1D11.16, ATCC Deposit Designation No. HB 9849 (page 6, paragraph [0015]).

Ledbetter does not teach a method of treating a mammal having diminished renal function, slowing loss of renal function in a mammal having a renal disorder or improving renal function in a mammal having diminished renal function, comprising administering to the mammal a therapeutically effective amount of a TGFß antagonist and a therapeutically effective amount of a RAAS antagonist to treat renal insufficiency, slow the loss of renal function or improve the renal function, respectively.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat a mammal having diminished renal function, slow loss of renal function in a mammal having a renal disorder or improve renal function in a mammal having diminished renal function, by administering to the mammal a therapeutically effective amount of a TGFß antagonist and a therapeutically effective amount of a RAAS antagonist, wherein the TGFβ antagonist is an anti-TGFβ antibody, as taught by Border and Reeves, and to modify that teaching by administering a human anti-TGFβ antibody, a humanized anti-TGFβ antibody, 1D11 or a humanized derivative of 1D11, as taught by Ledbetter, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification in order to neutralize TGFβ. The fact that Ledbetter's human anti-TGFβ antibody, humanized anti-TGFβ antibody, 1D11 and humanized derivative of 1D11 are known TGFβ antagonists in the art of renal therapy presents strong evidence of obviousness in substituting Ledbetter's antibodies in the method of Border and Reeves. The selection of a known TGFβ antagonist is prima facie obvious. The invention is prima facie obvious over the prior art.

Claims 1–8, 10, 13–19, 22–26, 28–30, 32 and 35–38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Border (Hypertension. 1998 Jan;31(1 Pt 2):181-8) and Reeves (Proc Natl Acad Sci U S A. 2000 Jul 5;97(14):7667-9) as applied to claims 1–4, 6, 13–19, 22–26, 28 and 35–38 above and further in view of Ledbetter (WO 01/66140) as applied to claims 1–4, 6–8, 10, 13–19, 22–26, 28–30, 32 and 35–38 above and further in view of Agarwal (Am J Kidney Dis. 2002 Mar;39(3):486-92).

Border and Reeves in view of Ledbetter teach a method of treating a mammal having diminished renal function, slowing loss of renal function in a mammal having a renal disorder or improving renal function in a mammal having diminished renal function, by administering to the mammal a therapeutically effective amount of a TGFß antagonist and a therapeutically effective amount of a RAAS antagonist, as discussed above. Border and Reeves in view of Ledbetter do not teach lisinopril.

Agarwal teaches that ACE inhibitor therapy is considered to confer renoprotection independent of systemic blood pressure (BP) (page 486, paragraph bridging left and right columns). The basis of selective renoprotective effects of ACE inhibitors and possibly ARBs has been linked to reduction of proteinuria, in addition to BP reducing effects of these agents (paragraph bridging pages 486-487). Agarwal teaches the administration of the ACE inhibitor lisinopril to patients with proteinuric nephropathies (Abstract). Agarwal does not teach a method of treating a mammal having diminished renal function, slowing loss of renal function in a mammal having a renal disorder or improving renal function in a mammal having diminished renal function, by administering to the mammal a therapeutically effective amount of a TGFß antagonist and a therapeutically effective amount of a RAAS antagonist.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to treat a mammal having diminished renal function, slow loss of renal function in a mammal having a renal disorder or improve renal function in a mammal having diminished renal function, by administering to the mammal a therapeutically effective amount of a TGFß antagonist and a therapeutically effective amount of a RAAS antagonist, as taught by Border and Reeves in view of Ledbetter, and to modify that teaching by administering a therapeutically effective amount of lisinopril, as taught by Agarwal, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because ACE inhibitors are renoprotective. The selection of a known ACE inhibitor is prima facie obvious. The invention is prima facie obvious over the prior art.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 9:00 A.M. TO 5:30 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, MANJUNATH RAO, CAN BE REACHED AT (571)272-0939.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300.

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING MAY BE OBTAINED FROM THE PATENT APPLICATION INFORMATION RETRIEVAL (PAIR) SYSTEM. STATUS INFORMATION FOR PUBLISHED APPLICATIONS MAY BE OBTAINED FROM EITHER PRIVATE PAIR OR PUBLIC PAIR. STATUS INFORMATION FOR UNPUBLISHED APPLICATIONS IS AVAILABLE THROUGH PRIVATE PAIR ONLY. FOR MORE INFORMATION ABOUT THE PAIR SYSTEM, SEE HTTP://PAIR-DIRECT.USPTO.GOV. CONTACT THE ELECTRONIC BUSINESS CENTER (EBC) AT 866-217-9197 (TOLL-FREE) FOR QUESTIONS ON ACCESS TO THE PRIVATE PAIR SYSTEM,

/DAVID S ROMEO/
PRIMARY EXAMINER, ART UNIT 1647

DSR
JUNE 23, 2008